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EXAMINER	
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1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/766,527.	BAB ET AL.	
	Examiner	Art Unit	
	Lora E. Barnhart	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-11,13-24,26-28,30 and 33-48* is/are pending in the application.

4a) Of the above claim(s) *5-7,19,26,27 and 38-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-11,13-18,20-24,28,30,33-37 and 46-48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/30/07 and the submission after final rejection received 10/1/07 have been entered.

Response to Amendments

Applicant's amendments filed 10/1/07 to claims 1, 3, 8-11, 13-15, 17, 18, 20-23, 26, 28, 30, 33-37, 46, and 48 have been entered. Claims 2, 12, 25, 31, and 32 have been cancelled in this reply. No claims have been added. Claims 1, 3-11, 13-24, 26-28, 30, and 33-48 remain pending in the current application. Prior art references not included with this Office action can be found in a prior action.

Election/Restrictions

Claims 5-7 were withdrawn from consideration by the examiner in the Office action mailed 9/7/06 pursuant to applicant's election on 6/29/06 of the species "Tyr-Gly-Phe-Gly-Gly" as required in the restriction requirement mailed 5/1/06. These claims remain withdrawn at this time.

Claims 38-45 were withdrawn from consideration by the examiner in the Office action mailed 10/30/06 pursuant to applicant's election on 9/26/06 of Group I as set forth in the restriction requirement mailed 9/7/06. In the 9/26/06 reply, applicants elected

without traverse claims drawn to methods requiring administration of a peptide to a patient, not those in which cells are contacted *ex vivo* with a peptide (see page 2 of the 9/7/06 restriction requirement). These claims remain withdrawn at this time.

The instant amendments to claims 19 and 26 cause the claims to be drawn exclusively to methods of contacting cells *ex vivo* with a peptide, i.e. to the matter of nonelected Group II. As such, claims 19, 26, and 27 are withdrawn from consideration and placed into nonelected Group II. Therefore, claims 5-7, 19, 26, 27, and 38-45 are/remain withdrawn from consideration.

Examination will continue at this time on claims 1, 3, 4, 8-11, 13-18, 20-24, 28, 30, 33-37, and 46-48 ONLY, to the extent they read on the elected species ("Tyr-Gly-Phe-Gly-Gly (SEQ ID NO:1)," "hematological disorders," and "myeloproliferative disorders") where applicable.

Claim Objections

Claim 30 objected to because of the following informalities: The word "hematopoietic" is misspelled at line 2. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4, 8-11, 13, 15-18, 20-24, 28, 30, 34-37, and 46-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Independent claims 1, 13, 20, 23, 46, and 48 recite the phrase "multilineage early CD34 positive stem cells," but this term is not particularly defined in the specification or the art. At page 19, paragraph 80, of the as-filed specification, various "early" cell subclasses are discussed in exemplary terms, but the specification fails to provide a sufficiently limiting definition of these cells. There is no basis in the claims for the relative term "early." It is not clear which cells are included in this limitation and which are not. Clarification is required. It is noted for the record that claims 3 and 14, which describe these cells in terms of marker expression, are not included in this grounds of rejection.

Because claims 4, 8-11, 16-18, 21, 22, 24, and 47 depend variously from indefinite claims 1, 13, 20, 23, 46, and 48 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 15 requires "selectively increasing the number of any one of the BFU-E and GEMM colony forming units," which is confusing for several reasons. First, the phrase appears to require that one particular CFU-GEMM be "increased in number," which is confusing. It is not clear whether this phrase requires that these CFU types proliferate. Furthermore, the basis for the "selective" increase is not pointed out; in other words, it is not clear what is not being increased while the BFU-E and GEMM CFUs are being so increased. The claim does not require, e.g., that the numbers of BFU-E and CFU-GEMM be increased while the number of some other type of CFU remains unchanged. Clarification is required. Because claims 16-18 depend in part on indefinite

claim 15 and do not clarify the issue, they must also be rejected under 35 U.S.C. § 112, second paragraph.

Claim 21 requires that the treatment of claim 20 be "in support of the treatment of the subject by bone marrow transplantation," which is confusing for several reasons. First, there is no antecedent basis in claim 20 for "the treatment of the subject by bone marrow transplantation." Second, it is not clear whether claim 21 actually requires that bone marrow transplantation be performed on the subject. Clarification is required.

Claim 28 is drawn to a treatment of "a subject" but then discusses a method in which YGFGG is administered to "a donor" whose stem cells are then obtained. It is not clear how the "subject" and the "donor" are linked in this method, if at all. Furthermore, claim 28 requires obtaining "a sufficient amount" of cells from the donor, but the claim does not set forth a particular purpose for which this amount must be sufficient. Clarification of both of these points is required.

Claim 30 is drawn to a method for "enhancement of engraftment of bone marrow transplants," but the method does not include any step in which bone marrow is transplanted to any subject. The scope of the claim cannot be determined. Clarification is required. Because claims 33-37 depend from indefinite claim 30 and do not clarify the point of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Claim 33 recites the limitation "the circulating early precursor double positive CD34/Flk2 cells," but there is no basis for this limitation in claim 30. Clarification is required.

Claim 34 recites the limitation "the immature cell and monocyte recovery," but there is no basis for this limitation in claim 30. Clarification is required.

Claim 35 recites the limitation "the BFU-E and GEMM colony forming units," but there is no basis for this limitation in claim 30. Furthermore, like claim 15, claim 35 refers to "selective" increase without pointing out the criteria for the selection. Clarification is required.

Claim 36 recites the limitations "the hematological reconstruction upon bone marrow transplantation" and "the cellularity of bone marrow," but there is no basis for these limitations in claim 30. Clarification is required.

Claim Rejections - 35 USC § 102

The rejections of record under 35 U.S.C. § 102 are withdrawn in light of the claim amendments unless specifically addressed below.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3, 4, 8, 13-15, 20, 21, 30, 33-37, and 46-48 are/remain rejected under 35 U.S.C. 102(b) as being anticipated by Bab et al. (1995, WO 95/00166; 1/29/04 IDS reference AC). The claims are interpreted for this rejection only as being drawn to various methods consisting of administering a peptide with the sequence Tyr-Gly-Phe-

Gly-Gly (SEQ ID NO:1; "YGFGG") to a subject suffering from a hematological condition. In some dependent claims, particular effects of the administration are pointed out.

Bab et al. teach administering YGFGG in phosphate buffered saline (PBS) to mice once a day for twelve days; on day 8, the mice were treated with a single X-ray radiation, and on day 14, the mice were sacrificed and their bone marrow isolated into PBS (Example 2; page 14, lines 7-26). Bab et al. further teach that the administration of YGFGG to mice stimulated the production of bone marrow cells (page 14, line 29, through page 15, line 5).

The discovery of a new use for an old structure based on unknown properties of the structure *might* be patentable to the discoverer as a process of using. *In re Hack*, 245 F.2d 246, 248, 114 USPQ 161, 163 (CCPA 1957). However, when the claim recites using an old composition or structure and the "use" is directed to a result or property of that composition or structure, then the claim is anticipated. *In re May*, 574 F.2d 1082, 1090, 197 USPQ 601, 607 (CCPA 1978) and *In re Tomlinson*, 363 F.2d 928, 150 USPQ 623 (CCPA 1966). See M.P.E.P. § 2112.02.

Bab et al. teach administering YGFGG to mice (Example 2). While Bab et al. do not teach all of the effects recited in claims 1, 8, 13, 15, 29, 30, 46, and 48, they do perform the same administration of YGFGG as in the present application (Examples 1, 3, and 4; paragraphs 00157, 00159, and 00160). Because the method steps (i.e. administration of YGFGG, which is termed "OGP(10-14)" in the instant application) are the same, Bab et al. inherently teach the same effects as those recited in claims 1, 8,

13, 15, 29, 30, 46, and 48. Bab et al. therefore anticipates the effects recited in claims 1, 8, 13, 15, 29, 30, 46, and 48 as instantly claimed.

To invalidate a patent by anticipation, a prior art reference normally needs to disclose each and every limitation of the claim. See *Standard Havens Prods., Inc. v. Gencor Indus., Inc.*, 953 F.2d 1360, 1369, 21 USPQ2d 1321, 1328 (Fed. Cir. 1991). However, a prior art reference may anticipate when the claim limitation or limitations not expressly found in that reference are nonetheless inherent in it. See *id.* and *Verdegaal Bros., Inc. v. Union Oil Co. of Cal.*, 814 F.2d 628, 630, 2 USPQ2d 1051,1053 (Fed. Cir. 1987). Under the principles of inherency, if the prior art necessarily functions in accordance with, or includes, the claimed limitations, it anticipates. See *In re King*, 801 F.2d 1324, 1326, 231 USPQ 136, 138 (Fed. Cir. 1986). **Inherency is not necessarily coterminous with the knowledge of those of ordinary skill in the art.** See *Titanium Metals*, 778 F.2d at 780. Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. See *id.* at 782. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new to the discoverer. See *id.* at 782 ("Congress has not seen fit to permit the patenting of an old [composition], known to others..., by one who has discovered its...useful properties."); *Verdegaal Bros.*, 814 F.2d at 633.

This court's decision in *Titanium Metals* illustrates these principles. See *Titanium Metals*, 778 F.2d at 775. In *Titanium Metals*, the patent applicants sought a patent for a titanium alloy containing various ranges of nickel, molybdenum, iron, and

titanium. The claims also required that the alloy be "characterized by good corrosion resistance in hot brine environments." *Titanium Metals*, 778 F.2d at 776. A prior art reference disclosed a titanium alloy falling within the claimed ranges, but did not disclose any corrosion-resistant properties. This court affirmed a decision of the PTO Board of Appeals finding the claimed invention unpatentable as anticipated. This court concluded that the claimed alloy was not novel, noting, "it is immaterial, on the issue of their novelty, what inherent properties the alloys have or whether these applicants discovered certain inherent properties." *Id.* at 782. This same reasoning holds true when it is not a property, but an ingredient, which is inherently contained in the prior art. The public remains free to make, use, or sell prior art compositions or processes, regardless of whether or not they understand their complete makeup or the underlying scientific principles which allow them to operate. The doctrine of anticipation by inherency, among other doctrines, enforces that basic principle." See *Atlas Powder Co. v. IRECO Inc.*, 51 USPQ2d 1943 (Fed. Cir. 1999).

Thus, a reference may be anticipatory if it discloses every limitation of the claimed invention either explicitly or inherently. A reference includes an inherent characteristic if that characteristic is the natural result flowing from the reference's explicitly explicated limitations. *Continental Can Co. USA, Inc. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991).

In the instant case, the effects recited in claims 1, 8, 13, 15, 29, 30, 46, and 48 flow from the administration of YGFGG to mice. The fact that Bab et al. did not

necessarily recognize each and every effect of said administration does not render the administration itself patentable.

Furthermore, Bab et al. anticipates claims 3, 14, 33-36, and 47 because these dependent claims do not further limit the steps recited within their respective independent claims *per se*, but rather describe effects of the steps. Therefore Bab et al. anticipates these effects for the reasons discussed above. Claims 9 and 30 require that the subject be undergoing irradiation; on day 8 of the method of Bab et al., the mice both irradiated and injected with YGFGG. Claims 20 and 21 require that the subject be suffering from a hematological disorder; this aspect is anticipated by the irradiated mice of Bab et al., which display low numbers of bone marrow cells (page 15, lines 1-2). Claim 28 requires obtaining "a sufficient amount" of stem cells from the treated subject, but since the claim does not particularly define any criteria for including a particular number of cells and excluding another or a requirement that the stem cells be purified to homogeneity, this claim is anticipated by the bone marrow isolation of Bab et al. (page 14, lines 22-23).

Response to Arguments

Applicants allege that the scope of the claims has been narrowed to require that the patient be undergoing chemotherapy and that stem cells be mobilized to peripheral blood, thus overcoming the rejection (Reply, page 11, last paragraph; and page 12, last paragraph). Applicants allege that the amendment to the claims requiring that the method "consist of" administering YGFGG to the patient overcomes the rejection

(Reply, page 13, first paragraph). These arguments have been fully considered, but they are not persuasive.

The claims have not been amended as applicant alleges; specifically, there is no requirement in any of the claims rejected under 35 U.S.C. § 102(b) over Bab that the patient be undergoing chemotherapy. In independent claims 1, 13, 15, 28, 30, 46, and 48, the patient may be "a subject receiving chemotherapy **or** suffering from hematological disorder." In independent claim 20, the patient may be "a subject suffering from any one of hematological disorders, solid tumors, immunological disorders and aplastic anemia **or** a subject suffering of [sic] any one of said disorders and receiving chemotherapy." It is noted that several dependent claims require that the subject be undergoing chemotherapy (specifically, claims 9, 10, 16, and 17), but none of these claims are rejected as being anticipated by Bab. As discussed previously, the mice treated by Bab are "suffering from a hematological disorder" in that they display low numbers of bone marrow cells (page 15, lines 1-2). Applicant seems to be advocating the importing of limitations from dependent claims into independent claims, which is improper.

Applicant alleges that narrowing the scope of the treatment methods from "comprising" the administration of YGFGG to "consisting of" such an administration overcomes the rejection over Bab, but it is not clear how such an amendment fails to be anticipated by the art. Bab teaches administering YGFGG to mice once daily for 12 days; Bab teaches that such an administration stimulates bone marrow production (see, e.g., Example 2 at page 14 of Bab). Bab conducts no additional administration or

treatment steps. It is not clear how the instant amendments overcome the art. Applicant has provided neither evidence nor argument that the administration of YGFGG taught by Bab (which, incidentally, is a regimen that appears to be nearly identical to that taught by applicants in the working examples) would not yield inherently the effects recited in the cited claims. Applicant has not pointed out, e.g., a step carried out in the treatment method of Bab that is specifically excluded by the instantly claimed treatment method that would materially affect the outcome of such a treatment method, or some conditions that are critical and were not acknowledged by Bab.

The majority of applicants' arguments of record regard whether the claimed effects are truly inherent effects of the recited YGFGG administration step. Applicants have presented no evidence that administering YGFGG as directed by Bab would not result in the claimed outcome. As discussed at length above, an inherent feature of an invention need not be recognized at the time of the invention. See M.P.E.P. § 2112. and *In re Schreiber*, 128 F.3d 1473, 44 USPQ2d 1429 (Fed. Cir. 1997). Applicants have not amended the claims to distinguish their patient set or administration step from that of Bab; such an amendment might overcome this ground of rejection.

Finally, it is not clear how applicant concluded that the examiner suggested an amendment of the claims to change "comprising" to "consisting of." No such suggestion was made in the Office action, and the examiner did not propose such claims as being allowable. The only explicit suggestion made by the examiner was that applicants amend the claims so as to distinguish their patient set or administration step from that of

Bab or that applicants provide evidence that administering YGFGG as directed by Bab would not result in the outcomes recited in the cited claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bab et al. (WO 95/00166) taken in view of Gazitt (2000, *Stem Cells* 18: 390-398; reference U). The claim is interpreted as being drawn to a method consisting of administering a peptide with the sequence Tyr-Gly-Phe-Gly-Gly (SEQ ID NO:1; "YGFGG") to a donor, then obtaining peripheral blood from said donor.

Bab teaches administering YGFGG in phosphate buffered saline (PBS) to mice once a day for twelve days; on day 8, the mice were treated with a single X-ray

radiation, and on day 14, the mice were sacrificed and their bone marrow isolated into PBS (Example 2; page 14, lines 7-26). Bab further teaches that the administration of YGFGG to mice stimulated the production of bone marrow cells (page 14, line 29, through page 15, line 5).

Bab does not exemplify isolating peripheral blood from the mice.

However, Bab teaches that the administration of YGFGG increases the number of hematopoietic totipotent cells and pluripotent stem cells in peripheral blood (page 9, line 29, through page 10, line 3).

Gazitt teaches that CD34 is a marker of peripheral blood stem cells, which are stem cells that regenerate the hematopoietic system (page 390).

A person of ordinary skill in the art would have had a reasonable expectation of success in obtaining peripheral blood from the mice of Bab because Bab teaches that methods for identifying peripheral blood from mice were well known at the time of the invention (page 4, lines 24-26). The skilled artisan would have been motivated to isolate peripheral blood from the mice treated with the method of Bab because Bab teaches that administration of YGFGG to mice increases the number of hematopoietic stem cells in the peripheral circulation, which are taught by Gazitt as expressing CD34, thus eliminating the need for marrow extraction to obtain stem cells.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to isolate blood containing $CD34^+$ stem cells from the mice treated using the method of Bab because Bab teaches that these methods were well known in the art and that the blood of mice so treated would have been reasonably

expected to include stem cells, and Gazitt teaches that mobilized peripheral blood stem cells were known at the time of the invention to express CD34.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant's comments regarding the obviousness rejections of record have been considered to the extent they apply to this new ground of rejection. Applicants allege that evidence has been provided that YGFGG has a "specific growth enhancing effect on [a] certain lineage of circulating early stem cells ($CD34^+$)," reciting numerous markers found allegedly only on particular cells (Reply, page 15, paragraph 2). Applicants comment on the promotion of BFU-E and GEMM colony formation by the claimed method (Reply, page 15, last paragraph, continued to page 16). Applicants make various comments about the Takayama reference (Reply, page 16, last paragraph, through page 17). These arguments have been fully considered, but they are not persuasive.

Claim 28 requires administering YGFGG to a donor (not to any patient suffering from any disorder) and obtaining peripheral blood therefrom. The majority of applicant's comments regarding the rejections of record discuss the effects of YGFGG in diseased individuals; such arguments are irrelevant to this rejection of claim 28.

Applicant's comments about the properties of the "circulating early stem cells" are the only comments that pertain to this ground of rejection. However, most of the comments at page 15, paragraph 2, recite markers that are not included in claim 28. Although the claims are interpreted in light of the specification, limitations from the

specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Gazitt provides ample teachings that the person of ordinary skill in the art would have had a reasonable expectation of obtaining peripheral blood comprising some $CD34^+$ cells from the mice treated with the method of Bab.

Claims 11, 18, and 22-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bab et al. (WO 95/00166) taken in view of Gurevitch et al. (1996, *Blood* 88: 4719-4724; reference A31 on 8/20/04 IDS) and Takayama et al. (1999, U.S. Patent 5,910,303). The claim is interpreted as being drawn to a method consisting of administering a peptide with the sequence Tyr-Gly-Phe-Gly-Gly (SEQ ID NO:1; "YGFGG") to a subject with a hematological disorder, in particular a myeloproliferative disorder, thereby increasing the number of CFU-GEMM and BFU-CFU-E in the subject.

The teachings of Bab et al. are relied upon as discussed above. Bab et al. do not teach treating myeloproliferative disorders or specifically increasing circulating early CD34+ stem cells or particular colony forming units (CFUs) in subjects with myeloproliferative disorders.

However, Bab does teach that the YGFGG peptide is the 5 C-terminal amino acids of osteogenic growth polypeptide (OGP) and that both YGFGG and full-length OGP promote bone marrow proliferation (see Examples 1 and 2, beginning at page 13).

Gurevitch et al. teach that administering OGP to mice increases the production of all types of white blood cells (Figure 1 and Table 2; see also page 4720, column 2, first paragraph under "Results"). This increase in white blood cell types is selective in that

Gurevitch teaches that the number of white blood cells is significantly increased by the administration of OGF; therefore, using the teachings of Gurevitch the skilled artisan can select whether or not to increase the number of white blood cells in a subject by selecting to administer OGF or not.

Takayama et al. teach treating myeloproliferative disorders, including myelofibrosis, with an agent that promotes platelet and leukocyte production and reversing the damage to bone marrow caused by radiation therapy (column 12, Examples 1 and 2).

A person of ordinary skill in the art would have had a reasonable expectation of success in increasing the numbers of CFU-GEMM and BFU-CFU-E in a subject administered the YGFGG of Bab because Bab teaches that OGP and YGFGG have similar effects on bone marrow proliferation (and, therefore, blood cell formation) and because Gurevitch teaches that the number of all types of white blood cells (and, therefore, the progenitors from which they came, the CFU-GEMM and BFU-CFU-E) are increased by administration of OGP.

The person of ordinary skill in the art would have had a further reasonable expectation of success in treating myeloproliferative disorders, including myelofibrosis, with the YGFGG of Bab et al. because Bab et al. teach that YGFGG stimulates bone marrow cell production and subsequent repopulation of the immune system (page 14, line 29, through page 15, line 5) and because Gurevitch teaches that administration of a molecule with similar activity promotes general enhancement of hematopoiesis. The

skilled artisan would have been motivated to so modify the invention for the expected benefit of treating myelofibrosis in a patient.

It would therefore have been obvious to a person of ordinary skill in the art at the time the invention was made to treat myeloproliferative disorders, including myelofibrosis, with the YGFGG of Bab et al. because Bab et al. teach that YGFGG stimulates repopulation of the immune system, because Gurevitch teaches that OGP (a peptide with function similar to that of YGFGG) increases hematopoiesis generally, and because Takayama et al. teach that such repopulation treats myeloproliferative disorders, including myelofibrosis.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant's comments regarding the obviousness rejections of record have been considered to the extent they apply to this new ground of rejection. Applicants allege that evidence has been provided that YGFGG has a "specific growth enhancing effect on certain lineage of circulating early stem cells ($CD34^+$)," reciting numerous markers found allegedly only on particular cells (Reply, page 15, paragraph 2). Applicants comment on the promotion of BFU-E and GEMM colony formation by the claimed method (Reply, page 15, last paragraph, continued to page 16). Applicants allege that since the YGFGG peptide does not affect platelets or leukocytes, the person of ordinary skill in the art would not have had a reasonable expectation of success at the time of the invention in treating the diseases discussed by Takayama (Reply, page 16, last

paragraph, through page 17). These arguments have been fully considered, but they are not persuasive.

First, as discussed above, most of the comments at page 15, paragraph 2, recite markers that are not included in claim 28. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant's comments about the effects of YGFGG on the number of CFU-GM are noted, but as discussed above in the rejection over 35 U.S.C. § 112, second paragraph, claim 15 provides no particular basis for the selectivity of increase in the recited CFU types. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). As pointed out above, the "selective" increase may come about as a result of the skilled artisan's decision to dose some mice with YGFGG and others with inactive saline.

Finally, applicant's comments about the teachings of Takayama regarding the mechanism of action of Takayama's treatment do not overcome this rejection. Takayama teaches that myeloproliferative disorders may be treated by administering an agent that promotes leukocyte (white blood cell) production. The teachings of Bab and Gurevitch indicate that the skilled artisan would reasonably have concluded at the time of the invention that YGFGG is such an agent. Therefore, the person of ordinary skill in the art would have been motivated to treat myeloproliferative disorders by administering YGFGG. See *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007).

Claims 9, 10, 16, and 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bab et al. (WO 95/00166) taken in view of Gurevitch et al. (1996, *Blood* 88: 4719-4724; reference A31 on 8/20/04 IDS) and Sager et al. (1992, U.S. Patent 5,154,921; reference A). The claim is interpreted as being drawn to a method consisting of administering a peptide with the sequence Tyr-Gly-Phe-Gly-Gly (SEQ ID NO:1; "YGFGG") to a subject undergoing chemotherapy for a hematological disorder.

The teachings of Bab et al. are relied upon as discussed above. Bab et al. do not teach treating subjects undergoing chemotherapy.

However, Bab does teach that the YGFGG peptide is the 5 C-terminal amino acids of osteogenic growth polypeptide (OGP) and that both YGFGG and full-length OGP promote bone marrow proliferation (see Examples 1 and 2, beginning at page 13).

Gurevitch et al. teach that administering OGP to mice increases the production of all types of white blood cells (Figure 1 and Table 2; see also page 4720, column 2, first paragraph under "Results"). This increase in white blood cell types is selective in that Gurevitch teaches that the number of white blood cells is significantly increased by the administration of OGF; therefore, using the teachings of Gurevitch the skilled artisan can select whether or not to increase the number of white blood cells in a subject by selecting to administer OGF or not.

Sager et al. teach that administering a polypeptide that increases the number of hematopoietic cells in bone marrow can be used to promote regeneration of

hematopoietic cells between cycles of myelotoxic chemotherapy (Abstract and column 10, lines 60-65).

A person of ordinary skill in the art would have had a reasonable expectation of success in treating a subject undergoing chemotherapy by administering the YGFGG of Bab because Bab teaches that OGP and YGFGG have similar effects on bone marrow proliferation (and, therefore, blood cell formation) and because Gurevitch teaches that the number of all types of white blood cells (and, therefore, the progenitors from which they came, the CFU-GEMM and BFU-CFU-E) are increased by administration of OGP. The skilled artisan would have been motivated to administer the YGFGG of Bab to a patient undergoing chemotherapy because Sager teaches that such a patient would require regeneration of hematopoietic cells and because Bab and Gurevitch teach that YGFGG and related molecule OGP increase hematopoiesis generally.

Therefore, the invention as a whole would have been *prima facie* obvious to a person of ordinary skill at the time the invention was made.

Applicant's comments regarding the obviousness rejections of record have been considered to the extent they apply to this new ground of rejection. Applicants allege that evidence has been provided that YGFGG has a "specific growth enhancing effect on certain lineage of circulating early stem cells ($CD34^+$)," reciting numerous markers found allegedly only on particular cells (Reply, page 15, paragraph 2). Applicants comment on the promotion of BFU-E and GEMM colony formation by the claimed method (Reply, page 15, last paragraph, continued to page 16). Applicants make numerous comments about the teachings of Takayama (Reply, page 16, last paragraph,

through page 17). These arguments have been fully considered, but they are not persuasive.

First, as discussed above, most of the comments at page 15, paragraph 2, recite markers that are not included in claim 28. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicant's comments about the effects of YGFGG on the number of CFU-GM are noted, but as discussed above in the rejection over 35 U.S.C. § 112, second paragraph, claim 15 provides no particular basis for the selectivity of increase in the recited CFU types. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). As pointed out above, the "selective" increase may come about as a result of the skilled artisan's decision to dose some mice with YGFGG and others with inactive saline.

Applicant has provided no comments regarding the particular suitability of YGFGG for treating patients undergoing chemotherapy.

Double Patenting

The double patenting rejections of record are withdrawn in light of the claim amendments.

No claims are allowed. No claims are free of the art.

Applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP

714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. Due to the procedure outlined in MPEP § 2163.06 for interpreting claims, it is noted that other art may be applicable under 35 U.S.C. § 102 or 35 U.S.C. § 103(a) once the aforementioned issue(s) is/are addressed.

Applicant is requested to provide a list of all copending U.S. applications that set forth similar subject matter to the present claims. A copy of such copending claims is requested in response to this Office action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is 571-272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lora E Barnhart
Patent Examiner